

Appl. No.: 10/690,462

Amendment dated August 24, 2005

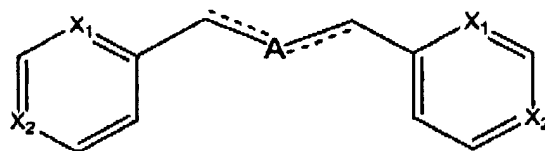
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Amendments to the Claims:

1-12 (Cancelled)

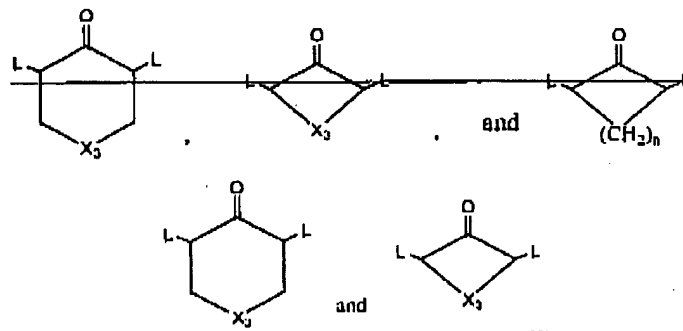
13. (Currently amended) A compound of the formula



wherein:

one of  $X_1$  and  $X_2$  is nitrogen and the other is carbon, wherein each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy,  $CF_3$ , alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, carboxylic acid, carboxylic ester, carboxamide, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

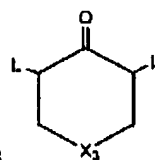
A is selected from the group consisting of:



wherein  $n$  is 1-8;  $X_3$  is O, S, SO,  $SO_2$ , or  $NR_1$ ; and  $R_1$  is selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl;

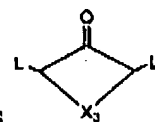
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the dashed lines indicate the presence of optional double bonds;  
L is the point of bonding of A to the compound structure; ~~and or~~  
a pharmaceutically acceptable salt thereof.



14. (Previously presented) The compound of Claim 13, wherein A is

15. (Previously presented) The compound of Claim 14, wherein  $X_3$  is S or  $NR_1$ .



16. (Previously presented) The compound of Claim 13, wherein A is

17. (Cancelled)

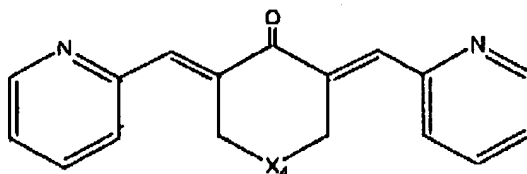
18. (Previously presented) The compound of Claim 13, wherein  $X_1$  is nitrogen.

19. (Previously presented) The compound of Claim 13, wherein  $X_2$  is nitrogen.

20. (Previously presented) The compound of Claim 13, wherein the optional double bonds are present.

21. (Currently amended) The compound of Claim 13, having the formula

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wherein:

$X_4$  is  $NR_1$ ;

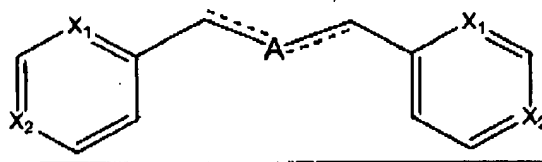
$R_1$  is selected from the group consisting of H, ~~alkyl~~, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl and dialkylaminocarbonyl;

each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy,  $CF_3$ , alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, carboxylic acid, carboxylic ester, carboxamide, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

and or a pharmaceutically acceptable salts salt thereof.

22. (Currently amended) The compound of Claim 13, ~~selected from the group consisting of~~ wherein the compound is 3,5-Bis-(2-pyridinylidene)-piperidin-4-one, 3,5-Bis-(2-pyridinylidene)-1-methylpiperidin-4-one, and 3,5-Bis-(4-pyridinylidene)-1-methylpiperidin-4-one.

23. (Currently amended) A pharmaceutical formulation, comprising a compound of claim 13 the formula



wherein:

one of  $X_1$  and  $X_2$  is nitrogen and the other is carbon, wherein each carbon atom of

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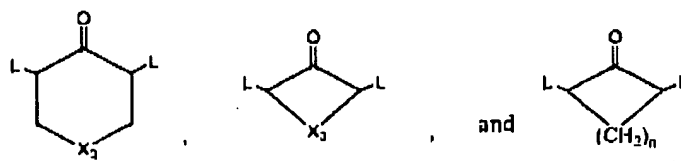
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the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF<sub>3</sub>, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, carboxylic acid, carboxylic ester, carboxamide, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

A is selected from the group consisting of:



wherein n is 1-8; X<sub>3</sub> is O, S, SO, SO<sub>2</sub>, or NR<sub>1</sub>; and R<sub>1</sub> is selected from the group consisting of H, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxy carbonyl, aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl;

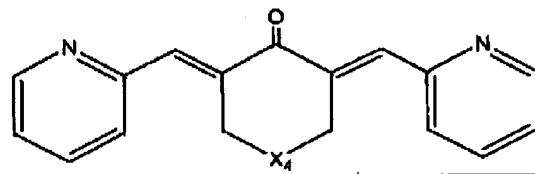
the dashed lines indicate the presence of optional double bonds;

L is the point of bonding of A to the compound structure; or

a pharmaceutically acceptable salt thereof;

and a pharmaceutically acceptable carrier.

24. (Currently amended) A pharmaceutical formulation according to claim 23, comprising a compound of ~~Claim 21~~ the formula



wherein:

X<sub>4</sub> is NR<sub>1</sub>;

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R<sub>1</sub> is selected from the group consisting of H, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl and dialkylaminocarbonyl;

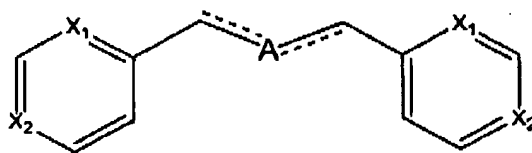
each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF<sub>3</sub>, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, carboxylic acid, carboxylic ester, carboxamide, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

or a pharmaceutically acceptable salt thereof;

and a pharmaceutically acceptable carrier.

25. (Currently amended) A pharmaceutical formulation according to claim 23, comprising a compound of Claim 22 3-5-Bis-(2-pyridinylidene)-piperidin-4-one, and a pharmaceutically acceptable carrier.

26. (Currently amended) A method of treating cancerous tissue in a subject, comprising administering to the subject an effective amount of a compound of formula



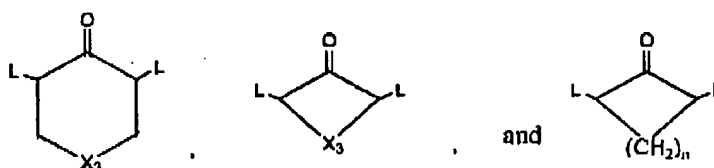
wherein:

one of X<sub>1</sub> and X<sub>2</sub> is nitrogen and the other is carbon, wherein each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF<sub>3</sub>, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, carboxylic acid, carboxylic ester, carboxamide, nitro, cyano, azide,

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alkylcarbonyl, acyl, and trialkylammonium;

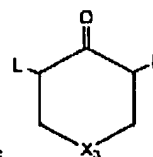
A is selected from the group consisting of:



wherein n is 1-8;  $X_3$  is O, S, SO,  $SO_2$ , or  $NR_1$ ; and  $R_1$  is selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl;

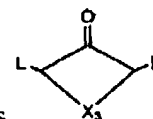
the dashed lines indicate the presence of optional double bonds;

L is the point of bonding of A to the compound structure; and or  
a pharmaceutically acceptable salt thereof.

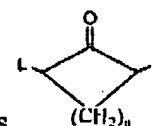


27. (Previously presented) The method of Claim 26, wherein A is

28. (Previously presented) The method of Claim 27, wherein  $X_3$  is S or  $NR_1$ .



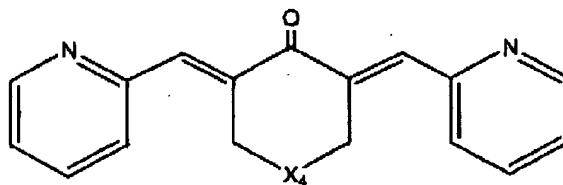
29. (Previously presented) The method of Claim 26, wherein A is



30. (Previously presented) The method of Claim 26, wherein A is  $(CH_2)_n$ , wherein n is 1-4.

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31. (Previously presented) The method of Claim 26, wherein  $X_1$  is nitrogen.
32. (Previously presented) The method of Claim 26, wherein  $X_2$  is nitrogen.
33. (Previously presented) The method of Claim 26, wherein the optional double bonds are present.
34. (Currently amended) The method of Claim 26, wherein the compound has the formula



wherein:

$X_4$  is  $NR_1$ ;

$R_1$  is selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxy, carbonyl, aminocarbonyl, alkylaminocarbonyl and dialkylaminocarbonyl;

each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy,  $CF_3$ , alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, carboxylic acid, carboxylic ester, carboxamide, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

and or a pharmaceutically acceptable ~~salt~~ salt thereof.

35. (Previously presented) The method of Claim 26, wherein the compound is selected from the group consisting of 3,5-Bis-(2-pyridinylidene)-piperidin-4-one, 3,5-Bis-(2-pyridinylidene)-1-

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methylnpiperidin-4-one, and 3,5-Bis-(4-pyridinylidene)-1-methylnpiperidin-4-one.

36. (Previously presented) A method of Claim 26, wherein the effective amount comprises an amount sufficient to inhibit VEGF production in the cancerous tissue.

37. (Previously presented) A method of Claim 26, wherein the effective amount comprises an amount sufficient to inhibit TF production in the cancerous tissue.

38. (Previously presented) A method of Claim 26, wherein said administering step comprises administering an effective amount of the compound in a pharmaceutically acceptable carrier.